

# **About the Cover**

Physicist James Hall prepares a test object for a neutron imaging experiment. He inserts a polyethylene core with machined "defects" into a brass and tungsten cylinder. The objective is to take a series of neutron radiographs through the cylinder and use them to reconstruct three-dimensional tomographs that reveal the structure of the polyethylene core. The article beginning on p. 4 describes experiments that are part of the effort to develop a neutron imaging system. Neutron imaging would complement x-ray imaging as a tool for nondestructively inspecting stockpiled nuclear weapons.



# **About the Review**

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May 2001

Lawrence Livermore National Laboratory

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# **Hubble data support MACHOs**

At the January meeting of the American Astronomical Society in San Diego, California, Livermore's Kem Cook and Cailin Nelson—reporting on behalf of the 14-organization collaboration to detect and study Massive Compact Halo Objects (MACHOs)—presented evidence of microlensing events caused by MACHOs in the halo of the Milky Way. Microlensing is a physical phenomenon that causes a star to appear to shift or brighten when it lies on the same line of sight as another star. The phenomenon is a way to detect MACHOs, which emit light below current detection thresholds and must therefore be discovered by other means. In MACHO microlensing, the MACHO passes through an observer's line of sight to an ordinary, luminous star. The MACHO's gravitational presence causes the light from the ordinary star to bend and also temporarily increase in brightness. That brightened star is called a source star.

The MACHO project has been monitoring the sky with the 1.27-meter telescope at Mount Stromlo Observatory in Australia to detect microlensing events in a line of sight toward our neighboring Large Magellanic Cloud galaxy, which provides a convenient backdrop of source stars. When the microlensing events were detected, some astronomers speculated that it was not MACHOs, but the faint stars in the Large Magellanic Cloud that were lensing other stars. If MACHOs are the cause of the microlensing, the source stars would be randomly distributed in the Large Magellanic Cloud, but if the source stars were found toward the far side of that galaxy, then the Large Magellanic Cloud would likely be the cause of microlensing.

To determine the cause of microlensing, the project collaborators turned to Hubble Space Telescope data on the area surrounding each microlensing event. Using the technique of difference image analysis, they were able to identify the source star of each microlensing event and therefore determine the arrangement of the source stars. The team found no evidence that the source stars are not randomly distributed in the Large Magellanic Cloud.

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# Over 150 high-proper-motion stars discovered

Also at the January meeting of the American Astronomical Association, astronomer Andrew Drake presented results from studying fifty thousand astronomical images of fifty-five million stars made by the Great Melbourne Telescope in Canberra, Australia, over a 7-year period. The telescope had been used during the 1990s to detect the gravitational microlensing of stars.

Drake reported finding 154 rapidly moving stars—called high-proper-motion (HPM) stars—toward the center of our galaxy and that of our brightest neighbor, the Large Magellanic

Cloud. This finding is of special interest because it is the first time that scientists have been able to discover HPMs in front of the stars seen at our galactic center, which is packed so densely with stars that images of the stars seem merged, or in the Large Magellanic Cloud, which appears as a faint nebulous patch in the sky.

To find the HPMs, Drake identified the stars that appear to move and measured their motions. The yearly motions of these objects are estimated to be accurate to 6 milliarcseconds, which is equivalent to the width of a human hair seen from the distance of a mile. Drake's measurements led to the discovery of the HPMs.

Using astrometry, a branch of astronomy that deals with the measurement of positions and movements and has produced a picture of the motions of stars within our galaxy, Drake was able to predict that most of his discovered HPM stars are between 100 and 1,000 light years away. These measurements, however, are preliminary, and more studies are needed to gather details about the HPM stars.

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# Lab enlisted in war against chemical weapons

At the behest of the U.S. State Department, Lawrence Livermore, home to the Forensic Science Center, has begun the procedure to become certified by the Organization for the Prohibition of Chemical Weapons (OPCW). The organization implements the Chemical Weapons Convention ratified by over 135 countries to outlaw chemical weapons and the transfer of chemical-weapon-related technologies. As an accredited laboratory, Livermore would participate in testing chemical samples from around the world to determine whether samples contain chemical weapons agents, their precursor chemicals, or their decomposition products.

Under the terms of the Convention, all chemical samples must be tested at two OPCW-designated laboratories. Congress mandates that all U.S. samples must be tested in the U.S. Currently, the nation has one designated laboratory, the Edgewood Chemical and Biological Forensic Analytical Center in Maryland. Livermore would become the second laboratory required for this testing.

Jeff Richardson, deputy program leader for the Proliferation Prevention and Arms Control Program, says that this work is "one more way the Laboratory can contribute to national and international security." Richardsons stresses that the samples for testing will "be extremely dilute (that is, on the part-permillion level). So dilute that they can be shipped commercially or sent through the mail." One of the reasons the Laboratory was selected for this work is its ability to characterize chemicals at ultratrace levels.

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# Advanced Technology for Stockpile Stewardship

NE of the greatest challenges facing Lawrence Livermore is helping to assure the safety and reliability of the nation's nuclear stockpile. This effort, called stockpile stewardship, demands our best technologies as well as our most creative thinking, especially in the absence of nuclear testing.

The Laboratory has been deeply involved in many aspects of stockpile stewardship. One of them is the Enhanced Surveillance Campaign, an effort to develop advanced diagnostic systems for the nondestructive surveillance of stockpiled nuclear weapons. Nondestructive surveillance is far more cost-effective and efficient than disassembling a weapon and its many components.

One of our most promising nondestructive surveillance technologies is described in the article beginning on p. 4. The article details how a team of Lawrence Livermore researchers is demonstrating the use of high-energy neutrons as a way to inspect thick, heavily shielded objects such as nuclear warheads. This technology is needed because current methods, such as x-ray imaging, cannot easily reveal defects in materials like plastics and ceramics when they are shielded by thick metal parts such as uranium.

The team has conducted experiments at Ohio University over the past four years. Because of the experiments' highly promising results, we hope to see a prototype system installed at Livermore that would ultimately be transferred to other National Nuclear Security Administration (NNSA) facilities.

Once in operation, high-energy neutron radiography's primary mission will be the surveillance of nuclear weapons. However, neutron imaging could also be used to perform such tasks as identifying warheads that need refurbishment or for inspecting refurbished warheads before they are returned to the stockpile. In this manner, the technology could serve as a valuable tool for carrying out any changes in the size of the nation's stockpile by helping scientists to make informed decisions based on the condition of weapons.

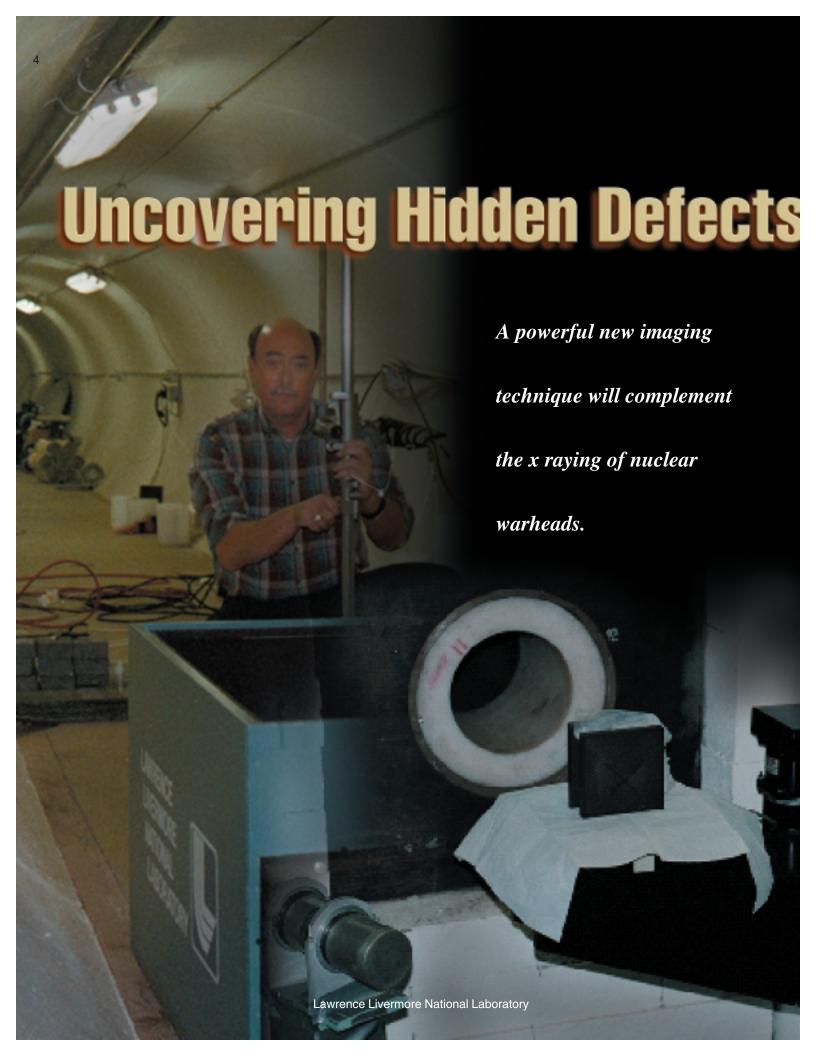
It is important to note that neutron imaging is designed to complement, not replace, existing nondestructive evaluation tools used in stockpile surveillance. In analyzing the state of the U.S. stockpile, researchers want as much data as they can possibly produce. Neutron imaging may be the only way that researchers can learn anything about the internal structure of some heavily shielded components. In this respect, neutron

imaging will simply help us do a better job of stockpile surveillance.

The success of high-energy neutron radiography demonstrates how we can leverage our experience in underground nuclear testing, which stopped in 1992. The initial idea for the project (that is, neutron imaging in the 10- to 15-megaelectronvolt energy range) and basic details of our current system design were derived from Monte Carlo simulations that used advanced neutron and gamma-ray transport codes first developed to support underground testing. Also, the design of the imaging detector is based on technology Livermore scientists originally developed for use at NNSA's Nevada Test Site.

High-energy neutron radiography is one of a number of enhanced nondestructive evaluation technologies under development at Lawrence Livermore. Another promising technology is high-energy x-ray tomography for high-resolution imaging of a nuclear warhead's plutonium pit. Our scientists are exploring other ideas as well, in response to high-level requests for new diagnostics that support stockpile stewardship. We hope these new ideas, like neutron radiography, will be successful so that they will also serve the nation's stockpile stewardship needs.

■ Jeff Wadsworth is Deputy Director for Science and Technology.



# with Neutrons

ROM the dentist's office to the aircraft hangar, the use of x rays to reveal the internal structure of objects is a time-honored practice. However, during the past few decades, several industries have begun to use thermal, or low-energy, neutron imaging as a complementary technique to x-ray imaging for inspecting objects without taking them apart. Now Lawrence Livermore researchers have demonstrated the power of using high-energy neutrons as a nondestructive inspection tool for evaluating the integrity of thick objects such as nuclear warheads and their components.

Experiments conducted over the past four years at Ohio University by a Lawrence Livermore team have demonstrated high-energy neutron imaging's considerable promise in probing the internal structure of thick

objects composed of materials that are essentially opaque to x rays. Indeed, the results have proven more successful than computer models first indicated or than Livermore physicists had expected.

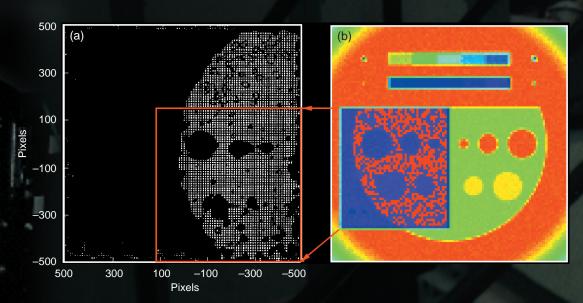
The neutron imaging project is funded through the Enhanced Surveillance Campaign, a key element of the nation's Stockpile Stewardship Program, which is managed by the National Nuclear Security Administration (NNSA) within the Department of Energy. Nondestructive surveillance—the search for anomalies from cracks to corrosion in aging stockpiled nuclear weapons systems to assure their continuing safety and reliability—is much more cost-effective than disassembling a warhead. Hence, the development of improved nondestructive surveillance techniques is crucial to the success of stockpile

stewardship in the absence of nuclear testing and to the nation's defense.

Nondestructive surveillance relies on a range of techniques, including x-ray imaging. X rays are adequate for inspecting the condition of parts composed of what scientists call high-Z (high-atomic-number) materials such as lead, tungsten, and uranium. However, x-ray imaging is not always effective in revealing voids, cracks, or other defects in so-called low-Z (low-atomic-number) materials such as plastics, ceramics, lubricants, and explosives when these materials are heavily shielded by thick, high-Z parts. (See the box on p. 6.)

# **Neutrons Complement X Rays**

Clearly, what is needed is a way to image shielded low-Z parts as a means to complement standard x-ray imaging



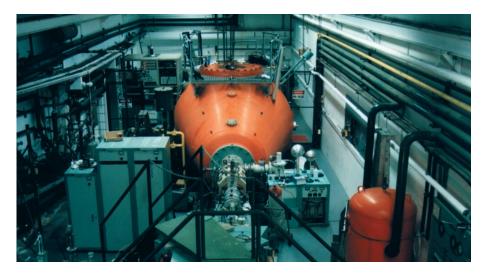
(a) Neutron image of an object with defects taken at the Los Alamos Neutron Science Center (LANSCE). (b) Computer simulations using Lawrence Livermore's COG Monte Carlo radiation transport code. The simulations show that neutron images taken at energy ranges between 10 and 15 megaelectronvolts could reveal defects in thickly shielded targets as well as LANSCE images, which were taken at much higher energies.

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of nuclear warhead components for stockpile surveillance. The answer seems to lie with high-energy neutrons, which are able to easily penetrate high-Z materials to interact with low-Z materials,

yielding clear, detailed images that are difficult to duplicate with x rays.

According to Lawrence Livermore materials scientist Jim LeMay, deputy program leader for Enhanced Surveillance,



Although larger in size than the proposed Lawrence Livermore neutron imaging system, the layout of the facility at the Ohio University Accelerator Laboratory in Athens, Ohio, is similar in configuration. The large orange vessel in the background is a Van de Graaff accelerator. It is used to accelerate deuterium ions into a cell containing deuterium gas to produce high-energy neutrons.

neutron imaging will be valuable to stockpile stewards on a number of fronts. He notes that weapons are randomly selected from the nation's nuclear stockpile for inspection. Neutron radiographs could be used as a means to screen these weapons and select one or more devices for complete disassembly and visual inspection. Also, neutron radiography could serve as a valuable inspection tool for identifying the warheads that actually need refurbishing as well as a valuable quality control tool for inspecting refurbished warheads before they are returned to the stockpile. Finally, neutron imaging of a statistically significant number of units could serve as a baseline assessment of the current state of a particular warhead.

Livermore physicist James Hall, the neutron imaging project leader, notes that imaging systems using thermal neutrons (average energy of about 0.025 electronvolt) are well established as nondestructive inspection tools in research and industry. However, these systems are generally limited to

# **A Neutron Primer**

All forms of radiation are attenuated (weakened) by a combination of slowing, scattering, and absorption processes as they pass through materials. The variation in attenuation through different parts of an object forms the basis for radiation imaging. The most widely used and commonly known form of radiation imaging is the x-radiograph in which an object is exposed to x rays and an image of the object (essentially a shadow) is recorded on photographic film or with a solid-state camera. Discovered more than 100 years ago, x rays today have a wide range of industrial and medical applications.

Neutrons, discovered in 1932, are electrically neutral particles similar in mass to a proton and present in the nuclei of all elements except hydrogen. Neutron imaging (conceptually similar to x-ray imaging) is commonly done today using neutrons that have an average energy of about 0.025 electronvolts. These neutrons are generated from fission neutrons produced in a nuclear reactor or from the decay of a radioisotope and then passed through thick layers of a hydrogen-rich material such as polyethylene to reduce their energy to thermal levels.

Most imaging applications using thermal neutrons exploit their strong interaction with hydrogen. For example, thermal neutrons can be used to inspect or detect explosives inside brass shell casings and search for corrosion in the aluminum skin of aircraft.

High-energy neutron imaging (for example, in the 10- to 15-megaelectronvolt range) is a relatively new technique that offers unique advantages over conventional x-ray and thermal neutron imaging, particularly for inspecting light (low-Z, or low-atomic-number) elements that are shielded by heavy (high-Z, or high-atomic-number) elements. These advantages are due in part to their greater penetrating power (that is, lower attenuation) through high-Z materials and, compared to x rays, their much stronger interaction (that is, higher attenuation) in low-Z materials.

Lawrence Livermore physicist James Hall emphasizes that neutron imaging yields different (and complementary) information to that obtained with x rays. "The use of one does not necessarily eliminate the need for the other," he says. Hall notes that although the ultimate spatial resolution attainable with high-energy neutron imaging—about 1 millimeter—is about 10 times less than the spatial resolution of x-ray imaging done with the most penetrating x-ray spectrum, it may be the only way that researchers can learn anything about the internal structure of some extremely thick objects.

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inspecting objects only a few centimeters thick. In the early 1990s, scientists at Lawrence Livermore and Los Alamos national laboratories speculated that higher-energy neutrons could be used to image much thicker objects such as nuclear warhead components.

Proof-of-principle tests began in 1994 at the Los Alamos Neutron Science Center (LANSCE), a facility that produces neutron beams with energies of up to 600 megaelectronvolts (MeV), far greater than those used by industry. The test object consisted of a 2.54-centimeterthick lithium deuteride (low-Z) disk that was sandwiched between two 5.08centimeter-thick uranium (high-Z) slabs. Small holes ranging from 4 to 12 millimeters in diameter were drilled all or part way through the lithium deuteride to simulate defects. A detector recorded images of the neutrons transmitted through the object from the LANSCE source with a spatial resolution of about 1 millimeter, revealing the presence of all of the holes.

# **Simulations Bolstered Confidence**

Encouraged by the success of these initial tests, Hall decided to model the LANSCE experiments using Livermore's three-dimensional Monte Carlo radiation transport computer code called COG. His computer simulations, however, focused on a lower energy range (10 to 15 MeV) because neutrons with these energies are known to penetrate high-Z materials effectively and yet interact more strongly with low-Z materials than the much higher-energy neutrons used at LANSCE. The COG simulations showed that neutron imaging in the 10- to 15-MeV energy range should be capable of revealing millimeter-size cracks, voids, and other defects in thick, shielded targets similar to the one tested at LANSCE.

Hall was also drawn to two other advantages of 10- to 15-MeV neutrons. The first is that neutrons in this energy range are much less expensive to generate than higher-energy neutrons such as those produced at LANSCE. Second, lower-energy neutrons are easier to detect because they allow the use of plastic scintillators, which are some 20 times more efficient than the conversion-type detectors required for much higher-energy neutrons.

One disadvantage of the lower energy range is the somewhat reduced penetrability of high-Z materials, which means exposure times of a few hours and sometimes longer are required for typical radiographs. However, says Hall, the greater detection efficiency and lower overall imaging costs more than make up for the longer exposure times.

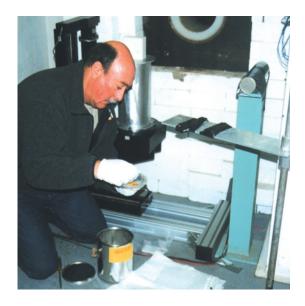
Following the computer simulations, Hall joined forces with colleagues Frank Dietrich, Clint Logan, and Brian Rusnak to design and develop a full-scale neutron imaging system for stockpile surveillance that would be capable of acquiring both radiographic (single-view) and full tomographic (three-dimensional) images. The system has to be relatively compact (about 15 meters long), both as a prototype suitable for installation and use at Livermore and in its fully developed form for eventual installation at other NNSA weapons complex facilities.

The resulting design features three primary components: an acceleratordriven neutron source generating an intense beam of 10-MeV neutrons, a remotely controlled staging system to support and manipulate objects being imaged, and a detector system with relatively high efficiency (about 20 to 25 percent) that can resolve defects of about 1 millimeter in diameter. To expedite the system's development and minimize technical risks, the team decided to use commercially available components and proven neutron imaging techniques wherever possible.

# **Ohio University Test Bed**

The team chose the Ohio University Accelerator Laboratory (OUAL) in Athens, Ohio, to evaluate the performance of a prototype imaging detector beginning in 1997. Although the accelerator facility at OUAL is much larger than that proposed in the Livermore design, its layout and configuration are similar. In addition, the OUAL staff has extensive experience in the production of accelerator-driven, high-energy neutron beams.

For the Lawrence Livermore experiments at OUAL, a 10-MeV neutron beam is generated by focusing deuterium ions into a cylindrical 1-centimeter-diameter by 8-centimeter-long deuterium gas cell attached to the end of the beam line. The gas cell is



Lawrence Livermore physicist
James Hall assembles a test
object called a sandwich
assembly for imaging at the Ohio
University Accelerator Laboratory.
Behind Hall is a prototype
multiaxis staging system that
secures and manipulates the test
object. On its way to the detector,
the neutron beam passes through
the test object and immediately
through a tapered polyethylene
collimator set into a 1.5-meterthick concrete and steel wall.

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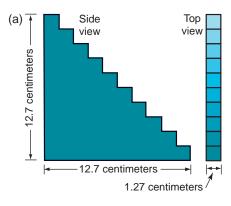
capped with thin entrance and exit windows and maintained at a pressure of about 3 atmospheres to limit the spread in energy of the resulting neutrons. The typical deuterium ion beam current

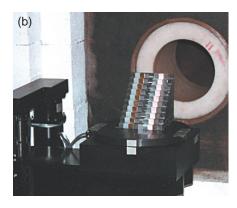
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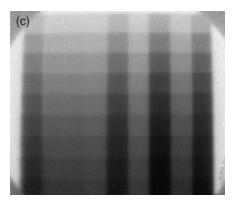
arriving at the gas cell is on the order of 10 microamperes, which corresponds to about 60 trillion ions per second. In comparison, Lawrence Livermore's proposed design will feature a

300-microampere accelerator with a 4-centimeter-long deuterium gas cell.

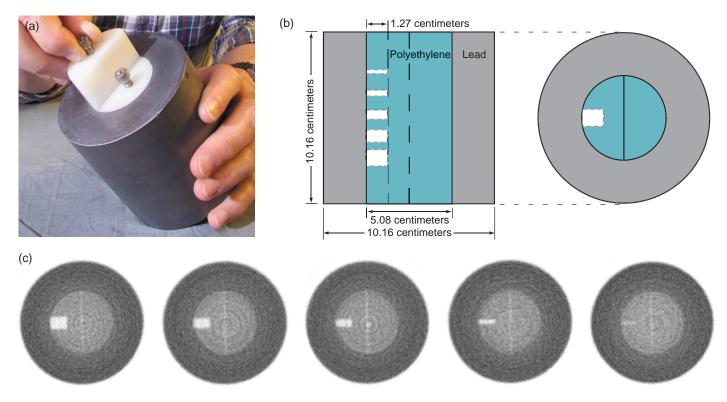
The result is a neutron beam flux only 15 times less intense than the intensity called for in the full-scale system. As a







(a) Nine step wedges fabricated from lead, Lucite, mock high explosive, aluminum, beryllium, graphite, brass, polyethylene, and stainless steel were imaged. Each step wedge has 10 steps ranging in thickness from 1.27 centimeters to 12.7 centimeters. (b) The nine wedges were imaged as a single unit. (c) The radiographs clearly differentiated the various materials and steps.



(a) A lead cylinder with a 10.16-centimeter outside diameter, a 5.08-centimeter inside diameter, and a polyethylene core was imaged. (b) The polyethylene core was split into two half-cylinders. One served as a blank, and the other had a series of holes that were 10-, 8-, 6-, 4-, and 2-millimeter-diameter by 1.27-centimeter-deep machined into its outer surface. (c) The resulting tomographic reconstructions clearly showed the core's structure, including the slight gap between the two halves.

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result, images take about 15 times longer to complete at OUAL than they will at Livermore. Nevertheless, the flux is sufficient to evaluate the performance of prototype detectors and for Lawrence Livermore researchers to gain valuable experience in neutron imaging. In many ways, says Hall, the Ohio University accelerator lab has been a "perfect test facility."

The experiments conducted thus far at OUAL have focused primarily on radiographic imaging of step wedges made of different materials and slab or sandwich assemblies, most with holes or other features machined into them to test the system's resolving power. The sandwich assemblies are typically composed of blocks of low-Z materials, such as polyethylene, that are shielded by various thicknesses of high-Z materials, such as lead or depleted uranium (D-38). Tomographic images of several cylindrical test objects composed of nested shells of high- and low-Z materials, with machined features, have also been obtained.

The test objects are mounted on a multiaxis staging system, which is located on the beam axis about 2 meters downstream from the neutron source and about 2 meters in front of the prototype imaging detector. The detector is housed in a shielded area behind a 1.5-meter-thick concrete and steel wall with a tapered polyethylene collimator to help minimize background radiation.

# Sandwiches, Steps, and Cylinders

One of the first experiments conducted at OUAL involved imaging a 12.7-centimeter-thick lead and polyethylene sandwich (with features machined into the polyethylene) and a set of 9 step wedges (see top figure, p. 8) fabricated from lead, Lucite, mock high explosive, aluminum, beryllium, graphite, brass, polyethylene, and stainless steel. Each step wedge had 10 steps ranging in thickness from 1.27 centimeters to 12.7 centimeters. The nine wedges were grouped together and radiographed as a single unit (looking up the steps from

thick to thin) in a series of two 1-hour exposures. The radiographs clearly differentiated the different materials and step thicknesses.

Another series of experiments involved imaging a 7.62-centimeter-thick D-38 and lithium deuteride sandwich (similar in design to the lead and polyethylene assembly previously described) and tomographic imaging of a lead cylinder with a 10.16-centimeter outside diameter, a 5.08-centimeter inside diameter, and a polyethylene core (see bottom figure, p. 8).

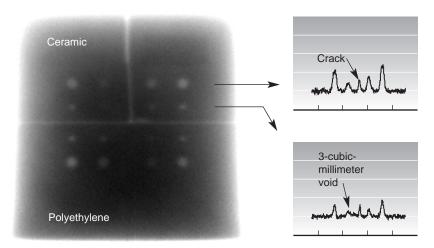
The polyethylene core was split into two half-cylinders. One served as a blank and the other had a series of holes machined into its outer (curved) surface that were 10, 8, 6, 4, or 2 millimeters in diameter by 1.27 millimeters deep. A series of sixty-four 10-minute exposures was taken of the cylinder at angles evenly distributed over 180 degrees. Resulting tomographic reconstructions clearly showed the core's structure. Although not well resolved, the narrow (less than 0.25-millimeter-wide) gap between the two halves of the polyethylene core was also visible in the reconstructed images.

Additional experiments at OUAL have focused on imaging objects made of other materials with a variety of machined

features. One object consisted of a 10.16-centimeter by 5.08-centimeter by 2.54-centimeter-thick slab of ceramic set atop a polyethylene slab of similar size and shielded by 2.54 centimeters of D-38. The ceramic piece featured two sets of 4- and 2-millimeter-diameter holes machined to depths of 4, 2, and 1 millimeters (the smallest hole corresponded to a defect with a volume of about 3 cubic millimeters). The ceramic was carefully cracked along its centerline and then reassembled so that the fracture was barely visible to the naked eye. The polyethylene piece featured the same set of 4- and 2-millimeter-diameter holes but no crack.

The object was imaged in a series of forty-eight 30-minute exposures. The final processed image and associated lineouts clearly showed the crack in the ceramic slab and all of the machined features, including the smallest 2-millimeter-diameter, 1-millimeter-deep hole.

Hall says the contact gap between the two ceramic pieces was probably less than 0.01 centimeter wide, far less than the designed resolution of the imaging system. Yet, the gap can still be resolved. "We're very pleased we can see this kind of detail through more than 2 centimeters



This neutron radiograph of a fractured ceramic and polyethylene test object shielded by 2.54 centimeters of depleted uranium shows the crack separating the two ceramic halves as well as a series of 4-millimeter-diameter (top) and 2-millimeter-diameter (bottom) holes machined into the ceramic. (A narrow slot was cut in the top of the ceramic to a depth of 2.54 centimeters to facilitate cracking the piece along its centerline.)

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# The Making of a Neutron Imaging System

The design of Livermore's neutron imaging system consists of a high-energy neutron source, a multiaxis staging platform to hold and manipulate an object, and an efficient imaging detector. The development of these components has proceeded in parallel over the past several years.

Neutrons can be produced using accelerators, radionuclides, or nuclear reactors. To achieve a high-energy neutron flux sufficient to image thick objects of interest within reasonable imaging times (a few hours), an accelerator-driven source appears to be the most practical option for stockpile surveillance purposes.

The accelerator, based on a commercially available design, will be built to Livermore specifications. The unit will focus a narrow (1.25-millimeter-diameter), pulsed (75-hertz), 300-microampere beam of deuterium ions into a 4-centimeter-long cell containing deuterium gas. (Deuterium is an isotope of hydrogen containing one proton and one neutron in its nucleus.) The collision of the deuterium ions with deuterium gas in the cell will produce an intense, forward-directed beam of neutrons with an energy of about 10 megaelectronvolts.

# **Collaborating with MIT**

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The combined requirements of a high deuterium-ion current and small beam diameter preclude the use of typical thin-walled ("windowed") deuterium gas cell designs. At an average power of about 170 kilowatts per square centimeter, the incident deuterium ion beam would generate far too much heat for any window material to withstand.

As a result, Lawrence Livermore researchers have teamed with nuclear engineering professor Richard Lanza at the Massachusetts Institute of Technology (MIT) to develop a "windowless" deuterium gas cell that can be efficiently coupled to a high-current, pulsed, deuterium accelerator. One design under consideration features a high-pressure (3-atmosphere) gas cell mounted at the exit port of a vacuum system. The cell's several pumping stages are isolated from each other by a series of rotating disks with small holes synchronized to the pulse frequency of the accelerator. In this way, the holes in the rotating disks line up about 75 times a second to allow the ion beam to

penetrate the cell without letting substantial amounts of deuterium gas leak out.

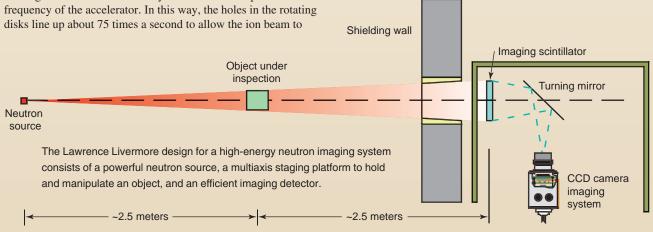
An alternative to the rotating aperture design is also being pursued by the Lawrence Livermore–MIT team. This approach, developed at Brookhaven National Laboratory, uses an intense plasma discharge to effectively plug the opening of the gas cell by rapidly heating and ionizing any deuterium leaking out. Similar "plasma windows" are being developed for use in electron-beam welding applications.

The object under inspection will be secured to a staging system that was originally designed at DOE's Y-12 Plant in Tennessee for x-ray imaging. The unit goes up and down and back and forth and rotates a full 360 degrees to permit both radiographic and tomographic imaging. Calculations and tests conducted at the Ohio University Accelerator Laboratory by Livermore researchers indicate that placing the staging system halfway between the source and the image plane of the detector will minimize the neutron scattering that can fog the image.

# **Imaging Detector Has Nevada Heritage**

The design of the imaging detector will be based on technology originally developed by Lawrence Livermore's Nuclear Test Program for use at DOE's Nevada Test Site. The full-scale detector will consist of a 60-centimeter-diameter transparent plastic scintillator viewed indirectly by a camera with a high-resolution (2,048- by 2,048-pixel) charge-coupled device (CCD) imaging chip.

A thin turning mirror made of aluminized glass will be used to reflect the brief flashes of light generated by neutrons interacting in the scintillator into the CCD camera, which will itself be located in a shielded enclosure well out of the neutron beampath. The camera will be fit with a fast (*f*/1.00 or better) lens to enhance its sensitivity and cooled with liquid nitrogen gas to –120°C to minimize thermal electronic noise.



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of uranium, even though we can't really quantify the gap," he says, adding, "we're seeing more than we ever expected."

Despite the experimental success enjoyed thus far, much work remains to be done to meet the goal of having a full-scale neutron imaging system in operation at Livermore by late 2003 or early 2004. Vendors need to be selected to build the accelerator, the detector's optics system, and the multiaxis staging system. Meanwhile, plans are under way to modify an existing Lawrence Livermore laboratory to house the system.

Once the system's performance is validated at Livermore, it will be transferred to other DOE facilities such as the Pantex Plant in Texas or the Y-12 Plant in Tennessee by late 2005 or early 2006. The continuing success of the Ohio University experiments makes it likely that neutron imaging will be serving the nation's stockpile stewardship needs within a few short years.

—Arnie Heller

Key Words: Brookhaven National Laboratory, COG Monte Carlo radiation transport code, deuterium, Enhanced Surveillance Campaign, lithium deuteride, Los Alamos Neutron Science Center (LANSCE), Massachusetts Institute of Technology (MIT), neutron radiography and tomography, Nevada Test Site, Ohio University Accelerator Laboratory (OUAL), Pantex Plant, scintillator, stockpile stewardship, x-ray imaging, x-ray radiography, Y-12 Plant.

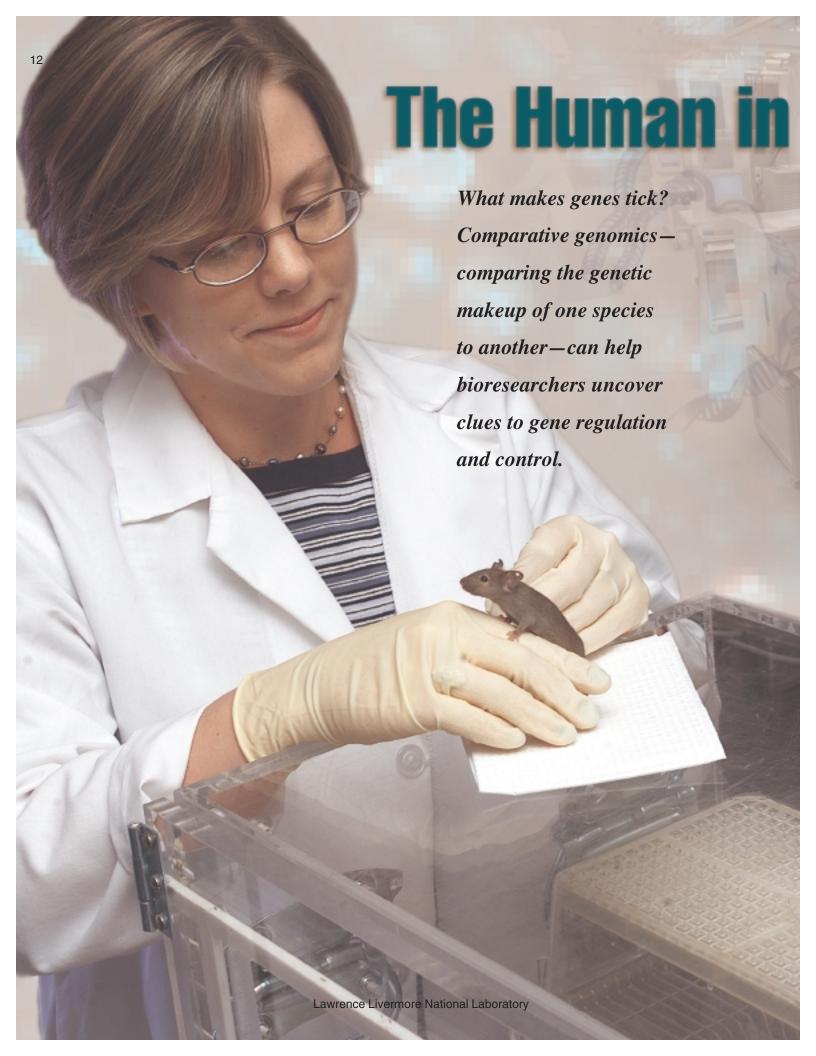
For further information contact James Hall (925) 422-4468 (jmhall@llnl.gov).

# **About the Scientist**



JAMES HALL received his B.S. in physics and mathematics from the University of Southern Colorado in 1974 and his M.S. and Ph.D. in physics from Kansas State University in 1977 and 1981, respectively. He joined Lawrence Livermore in 1987 as a physicist charged with the design and execution of nuclear device diagnostic experiments for the underground nuclear test program at the Nevada Test Site. With the end of underground testing

in 1992, Hall refocused his efforts on the development of detailed computer simulations of inertial confinement fusion diagnostics, flash x-ray systems, and nonintrusive luggage inspection systems. In 1994 he was selected to serve as the DOE representative and chief science advisor to the 8th Joint Compliance and Inspection Commission meetings associated with the Strategic Arms Reduction Treaty. Hall is currently a principal investigator for the development of high-energy neutron imaging techniques in support of stockpile stewardship.





N the excitement over the completed draft sequence of the human genome—certainly a grand accomplishment—it's easy to forget that this is just the prologue. Much about the genome remains a mystery. Which parts of it are actual genes? What do individual genes do, and how do they do it? (See the box on p. 17.) A small, four-footed mammal—the mouse—is helping to answer these questions. By comparing the human and mouse genomes piece by piece, bioresearchers such as Lawrence Livermore's Lisa Stubbs are uncovering clues to genomic mysteries.

After the draft sequence for the human genome was completed last June (see the box on p. 18), the Department of Energy's Joint Genome Institute (JGI) turned to sequencing pieces of mouse DNA that correspond to human chromosome 19. "We focused on this particular human chromosome because the Laboratory has created an extremely thorough gene map for it over many years of research," says Stubbs. "The sequence is not finished yet, but its working draft is easier to read than the draft sequence of many other human chromosomes. Because of the careful way the map was constructed, we know the sizes of the gaps in the

chromosome and the way the pieces fit together."

Since last October, when the mouse sequencing was completed, Stubbs and her team have been analyzing the mouse and human DNA sequences, examining both similarities and differences to discover what the sequences reveal about our genes and our genetic evolution.

Comparing the two sets helps the scientists track down genes—which are not always easy to spot—and provides information about the nongene portions of DNA that make up nearly 99 percent of our genome. Beyond that, having an understanding of why and how mouse and human genomes are different provides critical information to the bioscience and medical research communities. Stubbs explains, "If we're going to use the mouse as a model for the human, which everybody is doing, we'd better know how the two species differ and try to answer questions such as: How often do human and mouse contain the same genes? How similar are the genes? Are there exceptions to the rule of similarity? We must know these things on a gene-by-gene basis because while some genes are very similar, others are

not. Knowing all this will help us understand whether it's right to use mice for drug testing and as disease or drug models. And if it's not right, why not? Even the 'why nots' reveal something about the human gene and how it works."

# Junk, Shattered Genes, and a Twist

Two intriguing elements of the human genome came to light as a direct result of this comparative genomics: the different sizes of some related human and mouse regions and the composition of "junk" between the genes. Two pieces of related DNA for mouse and human show more or less the same genes in more or less the same order. But when Stubbs and her team spread out the two sequences and laid them side by side—the first time this has been done on a chromosome-wide scale—they discovered that many human regions are significantly larger and less compact than the mouse regions. So what's the filler in the human sequence? Scientists refer to it as junk, but not just any junk.

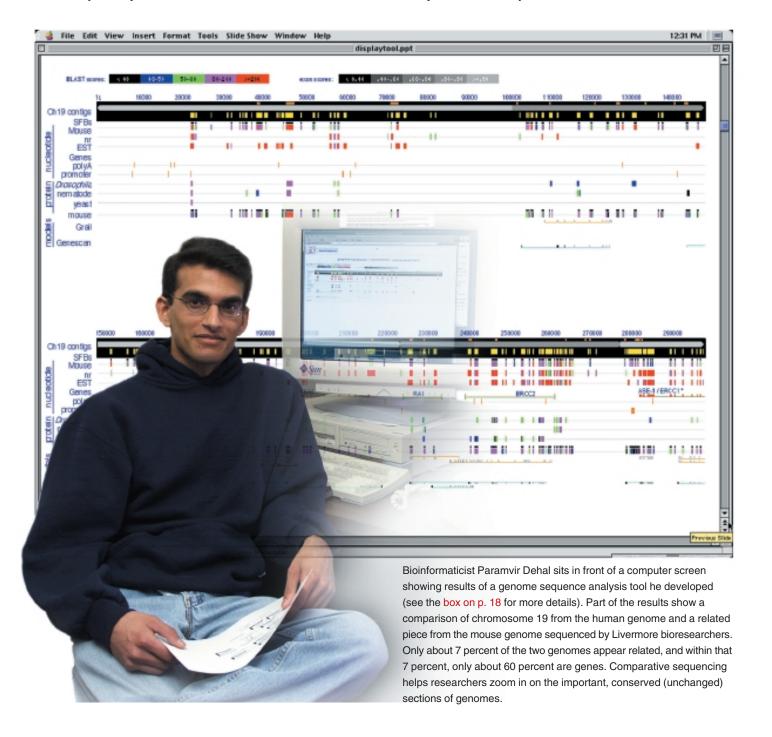
"For instance," Stubbs says, "there is a particular kind of junk sequence called the Alu sequence. It's a repetitive DNA sequence that, in the human, has made lots and lots of copies of itself and has Comparative Genomics S&TR May 2001

infected our DNA to a much greater extent than anything we see in mouse. It's just one of many DNA junk elements that make copies of themselves and litter the human genome in the millions."

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Repetitive sequences like Alus are essentially DNA parasites. Their

duplication generally does not appear to have serious functional consequences, although Alu copies that get inserted into genes have been shown to cause human disease. Stubbs notes that this sort of litter is also seen in mouse DNA. However, the Alu sequence invasion shows up more recently in the evolution of DNA and appears to have occurred more dramatically in the primate than the rodent lineages. Because mouse and human evolution haven't been separated all that many years, the difference in overall size and



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amount of junk is remarkable. "This is something we wouldn't have seen if we hadn't been able to lay out the pieces of sequence and compare them," she said. Why junk sequences happen and what they mean remain to be seen.

When the mouse and human sequences are compared, other broad similarities and differences quickly become apparent. Of the small percentage of the parts that make up genes, about 85 percent appear to be the same in sequence for both species. In addition, both mouse and human have basically the same number of genes generating more or less the same kinds of proteins. However, the genes lying on human chromosome 19 show up on several different mouse

chromosomes. It's as if someone shattered the human chromosomes and rearranged blocks of 20 to 200 genes into different orders to produce the mouse genome.

"This sort of rearrangement happens in evolution," says Stubbs, "but when we look at the genomes of other mammals that are just as far removed in evolution from the human as the mouse—the cat, dog, or cow—their chromosomes are much more similar to ours than the chromosomes from the rodent family. So what drives the breakup of mouse chromosomes? There are several theories, most concerning the short generation time and breeding habits of rodents, but what it comes down to is, we don't know yet."

In another interesting twist, when mouse and human genes were compared, quite a number of human-specific and mouse-specific genes were found. These species-specific genes are altogether a small fraction of our 30,000 genes, but still a significant number, probably several hundred genome-wide. "Weand nearly everyone else—expected to find a nearly one-to-one correspondence between mouse and human genes," says Stubbs. "The species-specific genes are of several different types, but the largest number of them appear to make or express regulatory proteins that do the actual business of turning genes on and off."

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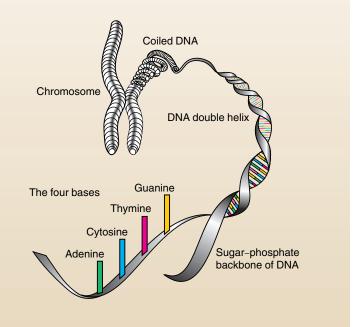
These proteins, continues Stubbs, are probably not critical, meaning that

# **Genome Basics**

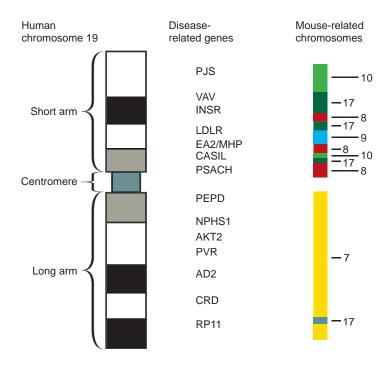
Each human cell contains 23 pairs of chromosomes in its nucleus. Each chromosome contains two tightly coiled strands of DNA (deoxyribonucleic acid), with each DNA strand composed of "base pairs" of chemical bases, normally abbreviated A, C, T, and G (for adenine, cytosine, thymine, and guanine). Scientists estimate that about 3 billion base characters comprise the human genome, with about 1.5 percent of those characters forming genes. Genes are special stretches of DNA that carry a code for making proteins, which are critical to helping our cells function. The process for making proteins is exact. Each cell contains complex proteins called transcription machinery. When it is time for a protein to be made, these machines go into the nucleus, find the control sequences that signal a particular gene to start, and bind to them. The transcription machinery then makes a mirror copy, or transcript, of the gene's sequence, as indicated by the control. The transcript, referred to as RNA (ribonucleic acid), then moves out of the nucleus and into the cell's cytoplasm where it encounters another biological machine, the ribosome. The ribosome, using the RNA as a set of instructions, assembles a protein from amino acids.

One way scientists identify genes is to capture RNA sequences in the cytoplasm and analyze them to determine which DNA sequences correspond to which RNA sequences. These captured RNA sequences are called complementary DNA (cDNA) sequences, and numerous collections of cDNA sequence snippets, called expressed sequence tags, are available in public databases. "A cDNA is a copy of the gene," explains

Livermore bioresearcher Lisa Stubbs. "Bioscientists have found ways to take RNA out of the cells, 'reverse transcribe' them into cDNA copies, clone them into bacteria, and sequence them. From the reverse transcription, we get a snapshot of the sequences in a particular cell that are being turned on and turned into proteins at a particular time."



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The human and mouse genomes are both similar and different. The long arm of human chromosome 19 has a close counterpart in mouse chromosome 7—the human and mouse versions of the same genes (see middle column) are found in them in roughly the same order. However, genes in human chromosome 19's short arm correspond to mouse versions that are located in many different mouse chromosomes, as indicated by the colored bars to the right, labeled by chromosome number.



Some of the members of the mouse genomics group are, from left, Laura Chittenden, Xiaojia Ren, Lisa Stubbs (team leader), Xiaochen Lu, Paramvir Dehal, and Joomyeong Kim.

gaining or losing them will probably not result in disaster to the organism. Instead, they probably are involved in fine-tuning traits. "These species-specific genes are very likely to be a major source of subtle diversity and keys to the subtle differences in gene expression between species," she says. Although the effects of changing a single gene are probably small, the combined effects of hundreds of changes are likely to be significant.

#### **What Makes Humans Human?**

Whether a gene resides on chromosome 2 or 20 usually does not affect its function. (The main exceptions to this rule are the genes on the sexlinked chromosomes X and Y.) That being said, scientists have to question why, with mice and humans having almost identical sets of 30,000 genes, they aren't more alike. Part of the answer is that a 15 percent difference in the sequence of a gene can change its function dramatically. For example, many human genes that cause disease differ from their normal counterparts by a single nucleotide. For most genes, this nucleotide change would constitute less than a 0.1-percent sequence change, but the result is a devastating functional difference.

Take the PEG3 gene, which is shared by mouse and human. It plays an important role in embryonic mouse development and an even more important role in mouse maternal behavior. Research shows that when the PEG3 gene is removed from mice, the mothers ignore their young to the point that their babies die. A similar protein is expressed in the human brain, says Stubbs, so the maternal caring function is probably conserved—unchanged during evolution—to some extent. "However, the levels of expression differ—the protein is expressed like gangbusters in the mouse brain, not so highly in the human. Even more intriguing, it's highly expressed in

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human ovaries and placentas, but not at all in mouse ovaries. It seems likely that this gene has taken on a role in humans that it isn't playing in mice."

Stubbs notes that many similar mouse and human genes have differing behavior: activated in one kind of tissue in mouse but not in human, or perhaps appearing in the same tissue in both, but at different times or with different intensities. "In other words, the same genes are not necessarily regulated or controlled in the same way in both species. The dissimilarities may be part of the answer as to why mice are mice and humans are human."

So what controls the on-off switch in genes and the timing of gene expression? Here again, rodents provide some clues. When researchers compare human and mouse sequences, they find small sections that are similar between the species but are not genes or junk such as Alus or other identifiable repetitive elements. Stubbs explains, "We can look at a piece of sequence and see that it isn't making part of a protein—so it isn't part of a gene. These mystery pieces, like genes, stand out as conserved DNA against a nearly

95-percent background of totally dissimilar sequence and are good candidates for a control sequence." Researchers know little about these types of sequences except that they are extremely important, hard to detect, and have been conserved because their sequence is linked to function. Many researchers are beginning to explore control sequences now that there is a way to find them through their conservation (because human and mouse genome sequences are known). Gene regulation, Stubbs says, is turning out be one of the most exciting areas of current research in the field.

# **Looking Section by Section**

Learning more about control sequences and other regulatory elements in gene expression is one of the next genomic frontiers. One technique used by the biomedical research community is tissue-section analysis, which is related to a standard hospital biopsy technique. The technique involves slicing 10-micrometer-thick sections of tissue (about the thickness of a single cell). It permits single cells to be viewed in their native context using

microscopy and standard pathological techniques.

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Adopting this technique, Stubbs and her team place thin slices of fetal or adult mouse tissue on a slide and add a gene probe, which is a specific gene sequence to which a fluorescent dye has been added. The probe binds to the unique RNA sequence produced by the gene under study. (The RNAribonucleic acid—is a mirror image of the DNA sequence of a gene and an intermediate in the process of protein coding.) When the tissue is observed under a microscope, the fluorescent probe can be seen binding to and highlighting the cells in which the particular RNA has been expressed. This technique of highlighting cells is called in situ hybridization.

Because a mouse fetus in even the latest stages of development is only about I centimeter long, its entirety can fit on a slide to give researchers a whole-body picture of where a particular gene is expressed. Stubbs explains, "Our pathologist Xiaochen Lu can look at a single specimen and tell us what cells are activated and what the purpose of those cells is. So if that gene is turned

# **Laying Out the Human Genome**

In February, the International Human Genome Sequencing Consortium—of which the Department of Energy's Joint Genome Institute (JGI) is a part—and the commercial company Celera simultaneously published papers in the scientific journals *Nature* and *Science* describing the draft sequencing of the human genome. The initial analysis of this draft sequence held a number of surprises. All in all, there appears to be only about 30,000 genes, equaling about 1 to 1.5 percent of the sequence. In other words, in the nearly 2-meter-long strand of DNA that appears in each and every cell of our bodies, about 15 centimeters of it contain genes. The number of genes is about a third to a half of what most scientists had believed would be the case. As Trevor Hawkins, JGI director, noted, "It puts us humans at something like about twice as many genes as your average fruit fly, which, I think, is quite a humbling thought."

Most of the leftover 99 percent of our DNA appears to be junk, or at least DNA whose functions remain unknown. Littered

in the junk are long sequences similar to those found in viruses and bacteria. These sequences appear to have taken up residence in the genome as far back as 700 million years ago, when life was composed of a single cell. "These sequences clearly have the structure of viral DNA," explains bioresearcher Lisa Stubbs, "but they've lost the ability to turn into a virus particle."

The International Human Genome Sequencing Consortium includes 20 groups from the United States, the United Kingdom, Japan, France, Germany, and China. Among those groups is the JGI, a virtual institute that integrates the sequencing activities of the human genome centers at Lawrence Livermore, Lawrence Berkeley, and Los Alamos national laboratories. For more information about the initial analysis and sequencing of the human genome by the International Human Genome Sequencing Consortium, see <a href="https://www.nature.com/genomics/human/">www.nature.com/genomics/human/</a>.

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# **Tools of the Comparative Trade**

Organizations such as the Joint Genome Institute (JGI) are extremely proficient in sequencing DNA, turning a task that used to be done painstakingly by hand a quarter century ago into an industrial procedure. However, analysis of that sequence—particularly comparing the sequence of two species—remains in the domain of human interpretation. Livermore bioresearcher Lisa Stubbs notes that there are computer programs to help scientists align the DNA sections of interest and to visualize similarities and differences. Computer algorithms can also identify a piece of DNA as a probable gene. But these tools are right only about 60 to 70 percent of the time and require human confirmation. Among the few computer tools available to help scientists visualize the differences and similarities between the sequence of two species are percent identity plots (PIPs) and dot plots.

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The PIP, developed by Webb Miller at Pennsylvania State University, is often used to find genes and regulatory elements. A scientist sends a file representing the bases of a piece of human sequence to the computer, followed by the piece of mouse DNA that corresponds to it. The program plots out the matches within the sections, marking matches with a dot and plotting them on a scale showing how similar the two sections are. Scientists can look along a stretch of DNA and quickly see that one piece is conserved—that is, hasn't changed during evolution—and then there's another little stretch of DNA that is somewhat less conserved and so on. The PIP program allows them to see how far apart those matches are. The program also can plot out positions of repetitive elements and find stretches of DNA that are rich in C and G bases. "We call these CpG islands," Stubbs explains, "Often, for some reason we don't yet understand, these islands are associated with control sequences. If you find an area rich in CpGs in both human and mouse, fairly close to a gene, it's a good candidate for a control sequence."

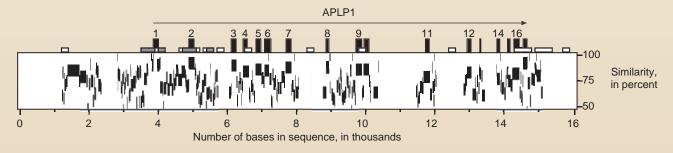
Dot plots are another tool that can be used to plot mouse DNA against the related piece of human DNA. In dot plots, the order of matching sequences of human and mouse DNA can be compared. Where the two aligned sequences match, a little mark is added to the graph. "This helps us see how the genomes align, where the similarities and differences in structure occur. For example, dot plots help us pinpoint the spots where the mouse chromosome has shattered, and half of it matches chromosome 19 and half matches

another human chromosome," Stubbs says. "It helps us find those breaking points."

Stubbs notes that tools such as PIPs and dot plots are slow and are better suited for looking at small pieces of sequence. At the JGI, Paramvir Dehal, a bioinformaticist and Ph.D. candidate in the Department of Genetics at the University of California at Davis, is working with Stubbs, computer scientist Art Kobayashi, and others to develop tools for examining and analyzing larger pieces of sequence. The tools they develop will be specifically designed as aids for comparative genomics. One sequence analysis tool being developed by Dehal uses a color code to show areas of similarity among various types of sequence, whether human, mouse, Drosophila (fruit fly), flatworm, yeast, or expressed sequence tags. A yellow bar along the chromosome map means the human DNA at that site has similarity to DNA from another species or to a recognized, previously studied human gene. Clicking on the bar brings up another screen that shows details of the sequence matches at that site and the degree of similarity between the matches, which is indicated by its colors. Red means an almost identical match; pink indicates a related sequence, but not a perfect match; and green or blue indicates that the matching sequence has few similarities to the human DNA.

Scientists can use this tool to find out which areas of the sequence are conserved among species. Areas of conservation usually indicate an important function, whether the area is a gene, regulatory sequence, or something else. "A pink match to *Drosophila* is truly significant because flies and humans are so far removed from each other in evolution. The likelihood is high that such a highly conserved piece of DNA is coding for a protein," Stubbs notes.

The tool is also handy for hunting down regulatory or control sequences. A piece of human sequence is a good candidate for a regulatory sequence if it matches mouse DNA, but not a cDNA sequence, and does not appear to be encoding a protein. Experiments must be done to verify the function of a conserved sequence because scientists presently cannot really predict a piece of DNA's function just by looking at its sequence. However, conservation does tell them which sequences are important and points them to the 1 to 5 percent of the genome they should focus on, which is an important first step.



A pip plot comparing the human APLP1 gene with its mouse counterpart. A high degree of similarity is shown between regions of human and mouse exons—the protein-coding DNA sequence of a gene. The exons are indicated by the black boxes at the top of the plot that are numbered from 1 to 16. The matches between human and mouse exons are marked by dots or lines. They indicate similarity generally over 75 percent.

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on in the heart, brain, and skin cells, we'll see the fluorescence in all those areas, in the exact cells that are activated. Finding out the exact cell type is important, because two cells that carry out the same function—say, secretion—may be more similar to each other than two different adjacent cells in the same tissue. For example, when we want to know what a gene does, it is much more important to know that the gene is expressed in a Purkinje cell, which helps regulate movement, than to know it's expressed somewhere in the

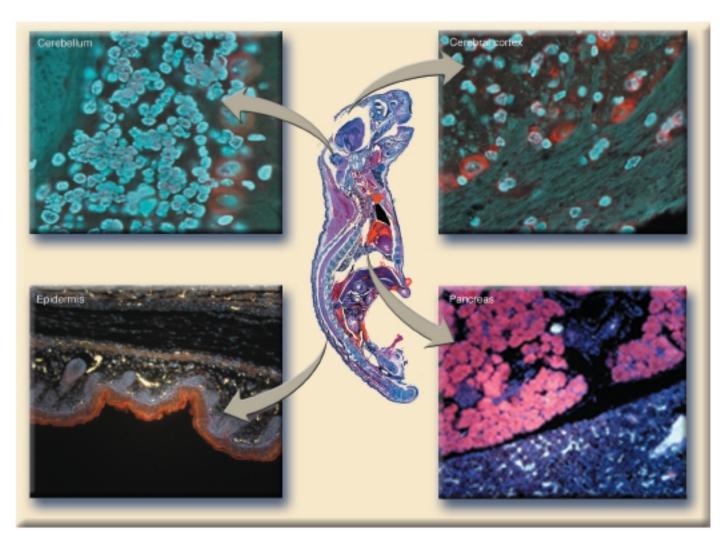
thousands of different cell types that make up the brain."

One gene that was examined in this manner turns out to be activated in only a small section of mouse sequence from a family line extensively studied by Stubbs, where the mice are prone to both deafness and stomach cancer. "What we found out about this gene through section in situ hybridization makes perfect sense to us," says Stubbs. "The gene expresses a protein that protects the epithelial cells lining the insides of body cavities, for example,

the stomach. The cells lining the inner ear are also delicate and may require the same kind of protection. We theorize that this same protein performs a similar protective function inside the ear. We haven't proved it, but we think that's why our mice are deaf and have stomach cancer."

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Because a single specimen provides 1,000 tissue slices, it can be used to test many genes. Stubbs and her team can create a probe of any gene found on the sequence—whether its purpose is known or unknown—and pinpoint



Thin slices of mouse tissue are placed on a slide, and a gene probe—a specific gene sequence with a fluorescent dye—is added. When the tissue is observed under a microscope, the fluorescent probe can be seen binding to and highlighting the unique gene sequence being studied. Here, this highlighting is shown for gene sequences in the cerebellum, cerebral cortex, epidermis, and pancreas.

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where it is expressed, down to type and location of a single cell, in the specimen.

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Elsewhere in the comparative genomics community, researchers are focusing on using microarrays to rapidly discover what genes express in tissues or tissue regions and to examine many genes in parallel. However, microarrays do not provide information about the type and location of a cell within a tissue that is expressing a gene or what that cell's context is in the living tissue. "With tissue-section-based techniques, we see exactly where a gene is turned on and can correlate it with the knowledge that pathologists have about what that particular cell does. We can also begin to correlate the state of the gene—its expression patterns in specific types of cells—with its regulatory sequences. This is completely unknown territory."

Stubbs and her team are working to industrialize this process. (See the box on p. 18.) With so many genes to look at, they need to generate a huge amount of information about gene expression to make generalizations about the genes and their regulatory controls. The team is now going through the sequence, looking and testing for candidate versions of these control sequences. "We're beginning to develop some testing techniques that will help us here. Ultimately, we want to go through the chromosome, find these control elements, prove that they are control elements, and then try to correlate expression patterns among them."

## **New Frontiers Within**

If nothing else, all the questions and possibilities just show that, even with the progress scientists have made in piecing together the story of life embedded in the DNA code, complete understanding still eludes them. "The human sequence means absolutely nothing when viewed by itself," notes

Stubbs. "We can do very little with it. We can find some of the genes from the expressed sequences we already know about. But we can't read it. We can't figure out where the important sequences are; we miss a lot of the genes; we miss all of the control sequences. What comparative sequence analysis allows us to do is to 'light up' the functional parts of the sequence. If a piece of DNA has an important function, evolution won't let it change. That's the important message in all this. But if we can't find the piece that is doing something important, we won't get very far in our understanding."

Why does this matter? Consider the gene tied to muscular dystrophy. When the gene is removed from the mouse, the mouse survives. It's a bit uncoordinated, Stubbs says, but it can move around, get on with its life, and reproduce. But when the gene is missing or malfunctioning in humans, the result is a disease of devastating proportions. "Obviously, this gene is much more important to humans

than to mice," says Stubbs. "And looking at the differences between the genes and the proteins and how they are regulated in mouse and human will help us understand what part of the human protein is most important. Now we'll be able to do the same sort of analysis for an entire chromosome, thanks to the mouse."

-Ann Parker

**Key Words:** chromosome 19, comparative genetics, DNA, Human Genome Project (HGP), gene expression, Joint Genome Institute (JGI), mouse genome, PEG3, sequencing, section in situ hybridization.

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For more information about DOE-funded genetic research, see these Web sites: www-bio.llnl.gov/genome/ www.jgi.doe.gov/ www.ornl.gov/hgmis/

# **About the Scientist**



**LISA STUBBS** received a B.S. in biology from the University of Puget Sound in Tacoma, Washington, and a Ph.D. in biology from the University of California (UC) at San Diego. She joined Lawrence Livermore in 1997 as a senior staff scientist in the Genomics and Bioengineering Research Division and in the DOE Joint Genome Institute, where Livermore is one of three collaborating national laboratories. She is currently also acting

director of the Genomics and Bioengineering Research Division.

Stubbs leads a team studying mouse genomics, specifically the comparative analysis of structure, function, and evolution of genes in related mouse and human chromosome regions. Her research interests include the generation, biological characterization, and molecular mapping of mouse mutants that provide useful models for studying acquired and inherited human diseases. Stubbs has published over 60 papers in professional journals and is on the editorial board of *Mutation Research Genomics*. She serves on several scientific committees, including the UC Davis Cancer Center Internal Advisory Board, the DOE Biology and Environmental Research Advisory Committee, and the National Institutes of Health Human Genome Study Section.

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neutrons and gamma rays. And when it's ready for experimental use, it must have 48 FOAs and nearly 100 diagnostic instruments mounted on its surface.

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When the chamber was designed in 1993, the design engineering team—led by Livermore's Vic Karpenko and Sandia National Laboratories' Dick Wavrik-consulted with laser scientists, optical experts, target physicists, laser physicists, and facility designers at Lawrence Livermore and Los Alamos national laboratories, the University of Rochester, and the Defense Threat Reduction Agency to come up with design requirements. The list of requirements included laser beams synchronized to arrive at the target simultaneously, fixed focal plane distances from the final optics to the targets, stringent vibration stability, and easy ingress and egress for systems that transport, hold, and freeze the tiny targets. The target chamber designers also had to consider space and cost constraints. Says Rick Sawicki, the laser area integration manager, "The world has made lots of spheres in the past, but all the requirements added together made the NIF target chamber a very challenging project, from an engineering perspective."

Requirements for the entire experimental system also affected the chamber and its subsystems. For example, the lasers must point at the target with extreme precision—on the equivalent of touching a single human hair from 90 meters away with the point of a needle. "Overall," says Sawicki, "we must deliver 1.8 megajoules of energy to the target with a 50-micrometer pointing stability on the target. That means we must accurately and stably point all laser beams and hold the target stable. Fifty micrometers is about the thickness of a sheet of paper, so that's how little wiggle room we have for any vibration in the system. Achieving that alignment on a table-top laser is one thing. Achieving it on a system the size of NIF . . . that's a huge challenge!"

The NIF teams analyzed all NIF structures to determine whether they could collectively meet the requirements. That analysis pointed to the target chamber as an important contributor to vibration. As a result, the target is not supported by the chamber but by a target positioner attached directly to the floor of the facility. Design features were implemented to permit the positioner to pass through the wall of the target chamber without coupling to the chamber's vibration, yet still maintain vacuum continuity. Throughout the facility, other steps were taken to dampen vibration and add stability. Concrete floors—nearly 2 meters thick in the Target Area Building and 1 meter thick in the Laser Building-help deaden stray vibrations. The target chamber is supported on a thick concrete pedestal and connected to the building floors at its waist to minimize vibration-induced motion. The Laser and Target Area Buildings will be temperature-controlled to 0.3°C to maintain laser

# **Pulsing the System**

Generating enough laser energy to cause fusion, thereby simulating the goings-on in the Sun and stars, is an exacting process.

From start to finish, each pulse of laser light must travel 450 meters before it reaches the target. That pulse begins humbly in the master oscillator system. A small fiber-ring oscillator generates a weak, single-frequency laser pulse on the order of a nanojoule. That pulse is launched into an optical fiber system that amplifies and splits it until there are 192 10-joule pulses.

The pulses enter the main laser system, where each light pulse makes four passes in a beampath of mirrors, lenses, amplifiers, switches, and spatial filters. This multipass concept was one of the design breakthroughs of NIF. Without it, the facility would have

Transport Booster amplifier spatial filter Cavity Cavity spatial amplifier filter Beam transport Preamplifier module Optical switch Lens **Target** Deformable Optical fiber mirror Frequency Beam Master oscillator conditioning/ converter (remote) debris shield

had to be over a kilometer long for the pulses to gain the required energy. In its multipass journey, each laser light pulse bounces off the equivalent of 54 mirrors and goes through the equivalent of 2 meters of glass. Each pulse is reflected off a deformable mirror to correct for aberrations that accumulate in the beam because of minute distortions in the optics. The mirror uses an array of actuators to create a surface that will compensate for the accumulated wavefront errors.

Once the beams have completed their passes through the main laser system, they proceed to two switchyards on either side of the target chamber. The switchyards take the 192 beams—which up to now have been traveling in bundles of 8 beams, 4 high and

2 across—and split them into quads of 2-by-2 arrays of beams. The quads are "switched" into a radial, three-dimensional configuration around the sphere. Just before entering the target chamber, each quad of pulses passes through a final optics assembly, where the pulses are converted from infrared to ultraviolet light and focused onto the target. The entire journey takes 1.5 microseconds.

S&TR May 2001 NIF Target Chamber

positioning. Sophisticated, low-vibration air-handling systems have been installed and are being activated.

# **Moving Right Along**

Work on the target chamber has continued apace since the chamber was lowered into the Target Area Building nearly two years ago (see S&TR, September 1999, pp. 16–19). Once the chamber was settled onto its massive concrete pedestal, workers used hydraulic jacks, roller assemblies, shims, and anchor bolts to align the chamber and establish its proper elevation and tilt. Then the chamber was leak-tested with helium gas. This testing had to be accurate because all the weld joints are covered by shielding material, which prohibits leak repairs. Next, the chamber was prepared for its shielding, a 40-centimeter-thick skin of gunite—a mixture of cement, sand, and water similar to that used to line swimming pools. The gunite was combined with 0.1 percent boron, a neutron-absorbing, activation-limiting material. Some 200 tons of the mixture was sprayed onto the chamber surface, which was then sealed with epoxy paint. NIF workers then opened the more than 70 ports for the FOAs and conducted a precision survey to pinpoint where all the laser beams would intersect.

"With all that concrete, we expected the chamber to sag somewhat," says Sawicki. That sagging would throw off the beam angles. Sagging also might be compounded by mounting the FOAs, which will add another 200 tons to the structure. Precision surveys have been performed to determine this impact as well. "Once everything is in place," says Sawicki, "we will make our final adjustments to the angle of the FOAs with simple spacers that can be accurately machined."

In the meantime, conventional construction throughout the facility has proceeded to 96 percent completion as of February 2001. Since the first of the year, both laser bays have been certified for clean room protocols; and vessel setting, steel framework fabrication, and installation of beampath infrastructure have begun. All in all, more than 11,500 metric tons of steel has been erected and more than 56,000 cubic meters of concrete has been poured.

# What's Next?

In February 2001, leak-testing was completed, and the target chamber was officially "in acceptance," that is, ready to accept the final optics assemblies, utilities, and diagnostics. "The chamber was designed for the lasers, the diagnostics, and the Target Area Building," notes Moses. "Completing it and putting it in place was an important stepping stone in building the project." In both the Laser and Target Area Buildings, the next major task is to install the beampath enclosures that connect the target chamber to all of the other vessels in the facility and to connect these enclosures to the utility systems (such as vacuum, helium, argon, compressed air, and water). All this will be accomplished while maintaining Level 100 cleanliness conditions inside the enclosures.

At the target chamber exterior, the surface of the vessel is prepared for an application of gunite. The shielding material is specially formulated to absorb neutrons and minimize radioactive induction in the aluminum chamber. At the National Ignition Facility, the Laser Building holds the two laser bays, which house most of the components of the main laser system; and

Elsewhere in the facility, 80 percent of the large components of the beampath infrastructure (such as vacuum vessels, support structures, beam tubes, and beam enclosures) have been procured and are either on the way or on site being installed. Over the next couple of years, the project will be making nearly \$1 billion in procurements of special equipment and putting it all together inside the space of the beampath enclosures. "The design of the facility is essentially done," Moses says. "Now, we need to turn from being an organization primarily focused on design and engineering to an organization focused on procurement, installation, and commissioning of the facility. That'll be our next big challenge."

the Target Area Building is divided into the switchyards, the target diagnostic

areas, and the target area. The target area, a circular space, contains the

target chamber and its attendant equipment.

-Ann Parker

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**Key Words:** chamber pedestal, design engineering, final optics assembly (FOA), laser amplification, Laser and Target Area Buildings, National Ignition Facility, precision survey, Stockpile Stewardship Program, target chamber, target positioner, vibration control.

For further information contact Richard Sawicki (925) 423-0963 (sawicki1@Ilnl.gov).

# **Indoor Testing Begins Soon at Site 300**

MAGINE, if you can, some 3,100 cubic meters of concrete and over 2,000 metric tons of reinforcing steel. "That's enough concrete and steel to build the frame of a 16- by 18-meter, 60-story office building," says Rick Visoria, project manager for the new Contained Firing Facility (CFF) at Site 300, Livermore's experimental test site. "Those are the quantities we used to build the firing chamber at the CFF, which is also 16 by 18 meters. But, it's only 10 meters high."

Those huge amounts of materials for a relatively small structure say a lot about the thickness of the firing chamber's concrete walls, the denseness of its reinforcing steel, and the thickness of its steel liners. Those thicknesses and densities are needed for tests inside that will use as much as 60 kilograms of high explosives—enough explosive to demolish that hypothetical 60-story building frame.

The inside surfaces of the firing chamber are protected by 50-millimeter-thick steel plates from a spray of shrapnel traveling as fast as 1.5 kilometers per second—that's three times the speed of a bullet. The chamber's main structural elements are designed to remain elastic when blasted by explosives, so that repetitive firings are possible.

The CFF, including the firing chamber, support area, diagnostic equipment area, and new offices and conference room, adds almost 3,200 square meters to Bunker 801 at Site 300. Bunker 801 houses the Flash X Ray—one of the most powerful x-ray machines in the world—and other diagnostic tools that have been used for many years to examine weapon components during hydrodynamic and other tests (see *S&TR*, March 1997, pp. 4–9, and March 1999, pp. 4–12).

Construction of the firing chamber and its support facilities began in April 1999 and was virtually complete by the end of 2000. Acceptance testing of the building and its many new systems is under way. During construction, Bunker 801 has been unusable, but by fall, its real work is expected to begin. The project's goal was to limit bunker downtime to 28 months. Says Visoria, "We'll be coming in almost exactly on schedule, and on budget, too."

The CFF will be an essential tool of the Department of Energy's Stockpile Stewardship Program to assure that our nation's nuclear arsenal remains safe and reliable as weapons age beyond their designed lifespan. Computer modeling provides considerable information about how a nuclear weapon will behave, but test data are needed to validate the codes used in modeling.



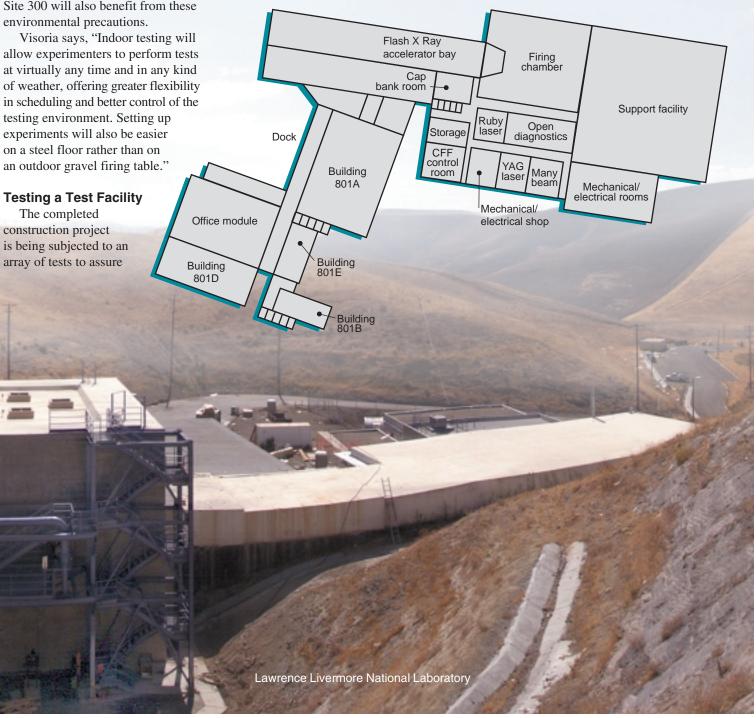
# Why Indoors?

Site 300 has been used since 1955 to perform experiments that measure variables important to nuclear weapon safety, conventional ordnance designs, and possible accidents (such as fires) involving explosives. To date, these experiments have been performed in the open air. The CFF will dramatically reduce emissions to the environment and minimize the generation of hazardous waste, noise, and blast pressures. While emissions from open-air testing at Site 300 are within current environmental standards, use of the CFF ensures that testing can continue even if environmental requirements change. Future residential development not far from

Site 300 will also benefit from these

that all systems are in working order. For example, tests are planned to assure that the CFF can withstand huge explosions of sometimes hazardous materials while remaining a safe place to work.

After construction was completed, Livermore personnel and the construction contractor, Neilsen Dillingham Builders Inc. of Pleasanton, California, conducted site acceptance tests of the CFF's state-of-the-art mechanical, electrical, safety, and process control systems. These tests culminated in the Firing Sequence of Operations, an integrated system test that checked out all the steps associated with firing an experiment. Several Firing





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(a) Aerial view of firing chamber construction on August 31, 1999, just prior to pouring the floor slabs for the firing chamber. This pour required deliveries by more than 100 concrete trucks. The protruding end of the Flash X Ray bullnose can be seen in the upper right. (b) The final concrete pour was for the roof slab of the firing chamber. Note the denseness of the reinforcing steel in both photos.

Sequence of Operations tests were run, sometimes under irregular conditions, such as when power to the facility was abruptly shut down.

The next step was the Structural Qualification Test Series to examine the integrity of the overall structure and the firing chamber in particular. A series of five high-explosive shots was conducted. The shots ranged from 25 to 125 percent of the explosive weight of 60 kilograms of high explosives. Data on the structural integrity tests are preliminary but indicate that all is well.

A spherical firing chamber structure would have been best for resisting blast effects. But a sphere is difficult to design and build because it does not use conventional construction methods. Engineering tests in the mid-1990s on a one-quarter-scale model of the firing chamber demonstrated that a rectangular, conventionally reinforced, concrete structure would have the structural strength to contain the blast effects of a high-explosive detonation. An essential requirement was that the chamber exhibit an almost totally elastic response to detonations within it, meaning that the chamber would not incur any permanent changes to its size or shape over time. Strain gauges installed in the thick walls, floor, and ceiling of the firing chamber are supplying the data needed to show that the full-scale facility meets the specified structural strength and elasticity response.

The last tests prior to putting Bunker 801 back to work will take about a month. They will assure that new CFF systems and those in the existing bunker are properly integrated.

### **Back to Work**

The CFF is the largest explosives chamber in the world. That means that no one at the Laboratory or anywhere else is experienced in bringing such a large indoor testing facility on line. Lloyd Multhauf, a deputy division leader in the Defense and Nuclear Technologies Directorate, which will be using the CFF, says, "Our first task will be to learn how to work with hazardous materials indoors. We will begin with less hazardous test shots and work up to those with more hazardous materials."

To purge the air in the firing chamber after a shot, the chamber is equipped with an air intake and exhaust system that can perform 10 air changes in half an hour. Exhaust air goes through a series of filters before being released into the atmosphere.

Personnel who then enter the firing chamber will be fully suited up to protect against any remaining hazardous materials. After removing the remains of the experiment, they will turn on a wash water system as necessary to remove any particulate matter from the walls and floor.

Says Multhauf, "Anyone entering the chamber will be in full personal protective equipment until we know for sure that the protective systems we've installed really operate properly."

There is much important work to do once Bunker 801 is fully operational. The Department of Energy recently assigned Livermore to perform work required to extend the lifespan of the W80 nuclear weapon, which was originally designed by Los Alamos National Laboratory. This effort will be similar to the W87 Life Extension Project that Livermore is completing. As design and engineering get under way to make the weapon more robust and able to withstand a longer time in the stockpile, hydrodynamic tests in the CFF will be numerous. But this time around, they will be indoors and much quieter.

-Katie Walter

**Key Words:** Contained Firing Facility (CFF), hydrodynamic testing, Site 300, Stockpile Stewardship Program, W80 Stockpile Life Extension Project.

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Each month in this space we report on the patents issued to and/or the awards received by Laboratory employees. Our goal is to showcase the distinguished scientific and technical achievements of our employees as well as to indicate the scale and scope of the work done at the Laboratory.

# **Patents**

# High Numerical Aperture Ring Field Projection System for Extreme Ultraviolet Lithography

Russell Hudyma

U.S. Patent No. 6,183,095 B1

February 6, 2001

An all-reflective optical system for a projection photolithography camera has a source of extreme ultraviolet (EUV) radiation, a wafer, and a mask to be imaged on the wafer. The optical system includes a first concave mirror, a second mirror, a third convex mirror, a fourth concave mirror, a fifth convex mirror, and a sixth concave mirror. The system is figured so that five of the six mirrors receive a chief ray at an incidence angle of less than substantially 12 degrees, and each of the six mirrors receives a chief ray at an incidence angle of less than substantially 15 degrees. Four of the six reflecting surfaces have an aspheric departure of less than substantially 7 micrometers. Five of the six reflecting surfaces have an aspheric departure of less than substantially 14 micrometers. Each of the six reflecting surfaces has an aspheric departure of less than 16 micrometers.

# Condenser for Ring-Field Deep-Ultraviolet and Extreme-Ultraviolet Lithography

Henry N. Chapman, Keith A. Nugent

U.S. Patent No. 6,186,632 B1

February 13, 2001

A condenser for use with a ring-field deep-ultraviolet or extremeultraviolet lithography system. A condenser includes a ripple-plate mirror that is illuminated by a collimated beam at grazing incidence. The ripple plate is a plate mirror onto which a series of channels has been formed along one axis to produce concave, undulating surfaces. Light incident along the channels is reflected onto a series of cones. The distribution of slopes on the ripple plate leads to a distribution of angles of reflection of the incident beam. This distribution has the form of an arc, with the extremes of the arc given by the greatest slope in the ripple plate. An imaging mirror focuses this distribution to a ring-field arc at the mask plane.

# High Numerical Aperture Ring Field Projection System for Extreme Ultraviolet Lithography

Russell Hudyma, David R. Shafer

U.S. Patent No. 6,188,513 B1

February 13, 2001

An all-reflective optical system for a projection photolithography camera has a source of extreme ultraviolet (EUV) radiation, a wafer, and a mask to be imaged on the wafer. The optical system includes a first convex mirror, a second mirror, a third convex mirror, a fourth concave mirror, a fifth convex mirror, and a sixth concave mirror. The system is configured so that five of the six mirrors receive a chief ray at an incidence angle of less than substantially 9 degrees, and each of the six mirrors receives a chief ray at an incidence angle of less than substantially 14 degrees. Four of the six reflecting surfaces have an aspheric departure of less than substantially 12 micrometers. Five of the six reflecting surfaces have an aspheric departure of less than substantially 12 micrometers. Each of the six reflecting surfaces has an aspheric departure of less than substantially 16 micrometers.

# Combined Passive Magnetic Bearing Element and Vibration Damper Richard F. Post

U.S. Patent No. 6,191,515 B1

February 20, 2001

A magnetic bearing system contains magnetic subsystems that act together to support a rotating element in a state of dynamic equilibrium and dampen transversely directed vibrations. Mechanical stabilizers are provided to hold the suspended system in equilibrium until its speed has exceeded a low critical speed where dynamic effects take over, permitting the achievement of a stable equilibrium for the rotating object. A state of stable equilibrium is achieved above a critical speed by a collection of passive elements using permanent magnets to provide their magnetomotive excitation. In an improvement over U.S. Patent No. 5,495,221, a magnetic-bearing element is combined with a vibrationdamping element to provide a single upper stationary dual-function element. The magnetic forces exerted by such an element enhance levitation of the rotating object in equilibrium against external forces, such as the force of gravity or forces arising from accelerations, and suppress the effects of imbalance or inhibit the onset of whirl-type rotordynamic instabilities. Concurrently, this equilibrium is made stable against displacement-dependent drag forces of the rotating object from its equilibrium position.

# Use of a Hard Mask for Formation of Gate and Dielectric Via Nanofilament Field-Emission Devices

Jeffrey D. Morse, Robert J. Contolini

U.S. Patent No. 6,193,870 B1

February 27, 2001

A process for fabricating a nanofilament field-emission device in which a via in a dielectric layer is self-aligned to a gate metal via structure located on top of the dielectric layer. A hard mask layer located on top of the gate metal layer is inert to the etch chemistry for the gate metal layer. In the hard mask layer, a via is formed by the pattern from etched nuclear tracks in a trackable material. The via formed by the hard mask will eliminate any erosion of the gate metal layer during the dielectric via etch. Also, the hard mask layer will protect the gate metal layer while the gate structure is etched back from the edge of the dielectric via, if such is desired. This method provides more tolerance for the electroplating of a nanofilament in the dielectric via and sharpening of the nanofilament.

# Laser Beam Temporal and Spatial Tailoring for Laser Shock Processing

Lloyd Hackel, C. Brent Dane

U.S. Patent No. 6,198,069 B1

March 6, 200

Techniques are provided for formatting laser pulse spatial shape and for effectively and efficiently delivering the laser energy to a work surface in the laser shock process. An appropriately formatted pulse helps to eliminate breakdown and generate uniform shocks. The invention uses a high-power laser technology capable of emitting the laser requirements for a high-throughput process, that is, a laser that can treat many square centimeters of surface area per second. The shock process has a broad range of applications, especially in the aerospace industry, where treating parts to reduce or eliminate corrosion failure is important. The invention may be used for treating metal components to improve strength and corrosion resistance. The invention has a broad range of applications for parts that are currently shot peened and/or require peening by means other than shot peening. Major applications for the invention are in the automotive and aerospace industries for components such as turbine blades, compressor components, and gears.

28 Patents S&TR May 2001

#### Implantable Medical Sensor System

Christopher B. Darrow, Joe H. Satcher, Jr., Stephen M. Lane, Abraham P. Lee, Amy W. Wang U.S. Patent No. 6,201,980 B1 March 13, 2001

An implantable chemical sensor system for medical applications is described that permits selective recognition of an analyte using an expandable biocompatible sensor, such as a polymer, that undergoes a dimensional change in the presence of the analyte. The expandable polymer is incorporated into an electronic circuit component that changes its properties (for example, frequency) when the polymer changes dimension. As the circuit changes its characteristics, an external interrogator transmits a signal transdermally to the transducer, and the concentration of the analyte is determined from the measured changes in the circuit. This invention may be used for minimally invasive monitoring of blood glucose levels in diabetic patients.

# NO<sub>x</sub> Reduction System Utilizing Pulsed Hydrocarbon Injection

Raymond M. Brusasco, Bernardino M. Penetrante, George E. Vogtlin, Bernard T. Merritt

U.S. Patent No. 6,202,407 B1

March 20, 2001

Hydrocarbon coreductants, such as diesel fuel, are added by pulsed injection to internal combustion engine exhaust to reduce exhaust  $NO_x$  to  $N_2$  in the presence of a catalyst. Exhaust  $NO_x$  reduction of at least 50 percent in the emissions is achieved with the addition of less than 5-percent fuel as a source of the hydrocarbon coreductants. By means of pulsing the hydrocarbon flow, the amount of pulsed hydrocarbon vapor (itself a pollutant) can be minimized relative to the amount of  $NO_x$  species removed.

# **Lightweight Flywheel Containment**

James R. Smith

U.S. Patent No. 6,203,924 B1

March 20, 2001

A lightweight flywheel containment composed of a combination of layers of various material that absorb the energy of a flywheel structural failure. The various layers of material act as a vacuum barrier, momentum spreader, energy absorber, and reaction plate. The flywheel containment structure has been experimentally demonstrated to contain carbon fiber fragments with a velocity of 1,000 meters per second and has an aerial density of less than 6.5 grams per square centimeter. The flywheel containment may, for example, be composed of an inner high-toughness structural layer, an energy-absorbing layer, and an outer support layer. Optionally, a layer of impedance-matching material may be used between the flywheel rotor and the inner high-toughness layer.

# Fabrication of Precision High-Quality Facets on Molecular Beam Epitaxy Material

Holly E. Petersen, William D. Goward, Sol P. Dijaili U.S. Patent No. 6,204,189 B1 March 20, 2001

Fabricating mirrored vertical surfaces on semiconductor layered material grown by molecular beam epitaxy (MBE). Low-energy, chemically assisted ion-beam etching is employed to prepare mirrored vertical surfaces on MBE-grown III–V materials under unusually low concentrations of oxygen in evacuated etching atmospheres of chlorine and xenon ion beams. Ultraviolet-stabilized, smooth-surfaced photoresist materials contribute to highly vertical, high-quality mirrored surfaces during the etching.

# **Awards**

Grant Logan was named director of the Heavy Ion Fusion Virtual National Laboratory (VNL) in early March, succeeding Roger O. Bangerter, who has retired. The Heavy Ion Fusion VNL is a collaborative venture of the Lawrence Berkeley and Lawrence Livermore national laboratories and the Princeton Plasma Physics Laboratory.

Logan, a member of the Physics and Advanced Technologies Directorate at Livermore, will be physically located at Lawrence Berkeley as he leads "heavy ion driver development and related topics in the common pursuit of inertial fusion energy (IFE)" and works "to promote more rapid progress in the development of heavy ion drivers through technical management integration of the laboratories' scientific staff, equipment, and experimental facilities."

Logan has worked in all parts of the U.S. fusion program. He was involved with both magnetic mirrors and tokamaks in Livermore's Magnetic Fusion Energy program and received the E. O. Lawrence Award in 1980 for coinventing the tandem mirror. He joined the Laser Directorate in 1992, where he worked in support of the National Ignition Facility and on heavy ion and laser IFE.

**Brendan Dooher**, an engineer in Livermore's Environmental Protection Department, is the first Laboratory employee to be selected for a **National Academy of Engineering fellowship**. He will spend a year in the nation's capital learning about and shaping science policy.

Dooher has been a key force behind GeoTracker, a geographic information system and database that provides online environmental data for tracking regulatory information about underground fuel tanks, fuel pipelines, and public drinking water supplies. The data are contributed by regulatory agencies and are used by both researchers and regulators to study groundwater contamination in California, in particular, contamination from MTBE that has leaked out of underground fuel tanks.

The Washington assignment is a fitting one for Dooher, who has a broad base of experience in many fields and disciplines. Likewise, his academic credentials include undergraduate and master's degrees in thermal systems and power plant design and a Ph.D. in probabilistic risk and systems analysis.

# **Uncovering Hidden Defects with Neutrons**

Experiments conducted over the past four years at Ohio University by a Lawrence Livermore team have demonstrated that high-energy (10- to 15-megaelectronvolt) neutron imaging holds considerable promise to probe the internal structure of thick objects. High-energy neutron imaging offers advantages over conventional x-ray and thermal neutron imaging, particularly for inspecting light (low-atomic-number) elements that are shielded by heavy (high-atomic-number) elements. The design of Lawrence Livermore's neutron imaging system consists of a powerful, high-energy neutron source, a multiaxis staging platform to hold and manipulate an object, and an efficient imaging detector. The work on this project is funded by the Department of Energy's Enhanced Surveillance Campaign, which is responsible for developing advanced nondestructive diagnostics for the surveillance of stockpiled nuclear weapons systems.

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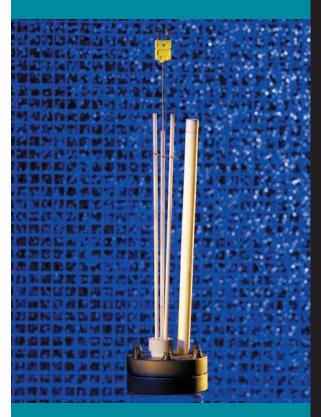
# The Human in the Mouse Mirror

The draft sequence of the human genome is complete, but work is just beginning on understanding what parts of the sequence are genes, what individual genes do, and how they do it. Lawrence Livermore bioresearcher Lisa Stubbs leads a group that is shedding light on the mystery of the human genome by comparing human and mouse genomes, piece by piece, focusing on chromosome 19. Using comparative genomic tools such as percent identity plots and dot plots developed at Livermore, they uncover the differences and similarities between the sequence of the two species, with intriguing results. They have found that only about 7 percent of the sequences are similar enough to be recognized as related. Many regions of the human genome are significantly larger than the corresponding regions in the mouse, with the human genome containing more "filler" sequences. Each species has a significant number of speciesspecific genes, many of which appear to be involved in regulating other genes. The sequences that control or regulate how genes act—when they produce proteins, where, and how much—is one of the next genomic frontiers that Stubbs and her team are researching.

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# Electricity Directly from Fossil Fuels



Livermore scientists are perfecting a new electrochemical process that converts carbon particles, derived from any fossil fuel, directly into electricity.

# Also in June

- Numerous environmental and earth sciences projects at Livermore are focusing on challenges of particular interest to California.
- Recently approved by the U.S. Food and Drug Administration, PEREGRINE goes to work providing improved radiation treatment of tumors.
- A soccer-ball-shaped nitrogen molecule promises to become a powerful new fuel or propellant.

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